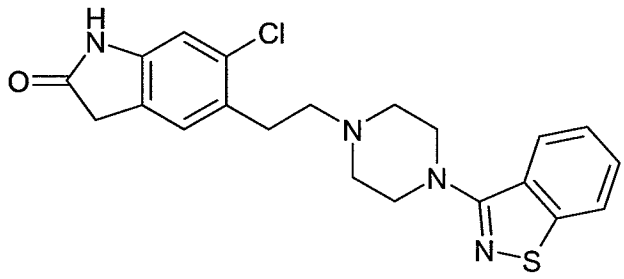
AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended): A process for preparing 5-[2-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl] ethyl]-6-chloro-1,3-dihydro-2H-indol-2-one (ziprasidone) of the formula I:

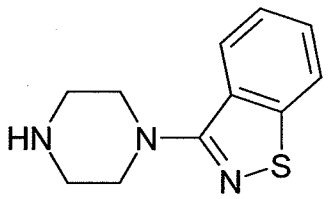
~~Ziprasidone of formula (I):~~



---------- I

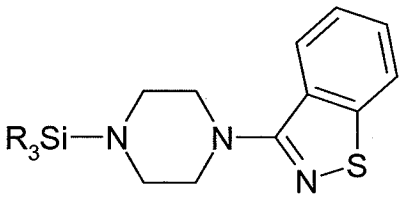
or a pharmaceutically acceptable salt thereof; or a solvate or a hydrate thereof.; which comprises:

a) silylating 1-(1,2-benzisothiazol-3-yl)piperazine of the formula II:



---------- II

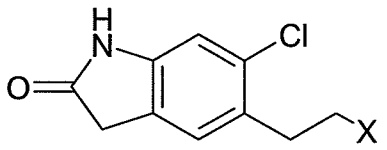
with a silylating agent to form a compound of the formula III:



---------- III

wherein R is independently alkyl;

b) reacting the silyl compound of the formula III with a 5-(2-haloethyl)-6-chloro-oxindole compound of the formula IV:



---------- IV

wherein X is fluoro, chloro, bromo or iodo;

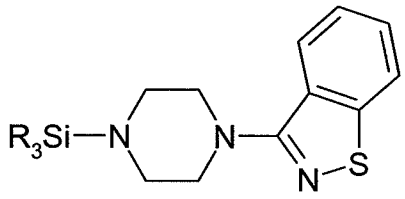
in a solvent in the presence of a base to neutralize the hydrohalic acid, at about 40^0C to the reflux temperature of the solvent used to form the compound of formula I and optionally converting the compound of formula I into a pharmaceutically acceptable acid addition salt thereof, or a solvate or a hydrate thereof.

2. (Previously Presented): The process according to claim 1 wherein the silylation step(a) is carried out with a silylating agent in the presence of a solvent and a tertiary amine base.
3. (Previously Presented) The process according to claim 2 wherein the silylating agent is selected from trialkylsilyl halides, N,O-bis(trimethylsilyl)-acetamide and N,N'-bis(trimethylsilyl)-urea.
4. (Previously Presented): The process according to claim 3 wherein the silylating agent is selected from trialkylsilyl halides.
5. (Previously Presented): The process according to claim 4 wherein the silylating agent is a trialkyl silyl chloride.
6. (Previously Presented): The process according to claim 3 wherein the silylating agent is selected from trimethylsilyl chloride, triethylsilyl chloride, N,O-bis(trimethylsilyl)-acetamide and N,N'-bis(trimethylsilyl)-urea.
7. (Previously Presented): The process according to claim 6 wherein the silylating agent is trimethylsilyl chloride.
8. (Previously Presented): The process according to claim 1 wherein the solvent used in the silylating step(a) is selected from ethyl acetate, methyl acetate, isopropyl acetate, tert-butyl methyl acetate, ethyl formate, acetonitrile, dimethylsulfoxide, dioxane, cyclohexane, n-hexane, benzene, toluene, xylene, methylene chloride, chloroform, carbontetrachloride,

ethylene dichloride, acetone, methyl ethyl ketone, methyl isobutyl ketone, diethyl ketone, tert-butyl methyl ether, diethyl ether, diethyl carbonate, and a mixture thereof.

9. (Previously Presented): The process according to claim 8 wherein the solvent is selected from methylene chloride, ethylacetate, cyclohexane, ethylene dichloride and a mixture thereof.
10. (Previously Presented): The process according to claim 9 wherein the solvent is methylene chloride.
11. (Previously Presented): The process according to claim 1 wherein X of the compound of formula IV is chloro, bromo or fluoro.
12. (Previously Presented): The process according to claim 11 wherein X is chloro.
13. (Previously Presented): The process according to claim 1wherein the solvent used in step(b) is selected from ethyl acetate, methyl acetate, isopropyl acetate, tert-butyl methyl acetate, ethyl formate, methanol, ethanol and isopropyl alcohol, acetonitrile, tetrahydrofuran, dimethylformamide, dimethyl sulfoxide, dioxane, cyclohexane, n-hexane, benzene, toluene, xylene, methylene chloride, chloroform, carbontetrachloride, ethylene dichloride, acetone, methyl ethyl ketone, methyl isovutyl ketone, diethyl ketone, tert-butyl methyl ether, diethyl ether, diethyl carbonate, water and a mixture thereof.
14. (Previously Presented): The process according to claim 13 wherein the solvent is selected from dimethylformamide, methylisobutylketone, water or a mixture thereof.
15. (Previously Presented): The process according to claim 1 wherein the base used to neutralize hydrochloric acid is selected from alkaline metal carbonates, alkaline metal bicarbonates, anhydrous ammonia, aqueous ammonia, pyridine, hydrides and tertiary amines.
16. (Previously Presented): The process according to claim 15 wherein the base is selected from sodium carbonate, potassium carbonate, sodium bicarbonate, potassium bicarbonate, triethylamine and diisopropylethylamine.
17. (Previously Presented): The process according claim 16 wherein the base is sodium carbonate or potassium carbonate.
18. (Previously Presented): The process according to claim 1, wherein the reaction is carried out at about 50^0C to the reflux temperature of the solvent used.

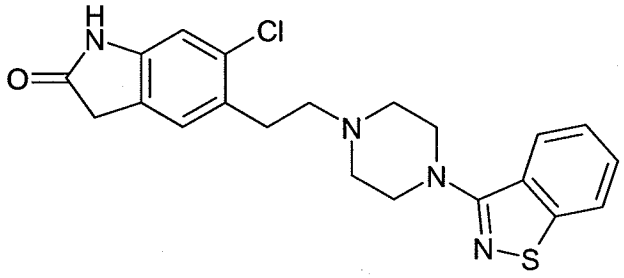
19. (Previously Presented): The process according to claim 18 wherein the reaction is carried out at about 80^0C to the reflux temperature of the solvent used.
20. (Previously Presented): The process according to claim 19 wherein the reaction is carried out at the reflux temperature of the solvent used.
21. (Previously Presented): The process according to claim 17 wherein the base is sodium carbonate.
22. (Previously Presented): The compound of the formula III:



---------- III

wherein the R_3 groups are independently alkyl.

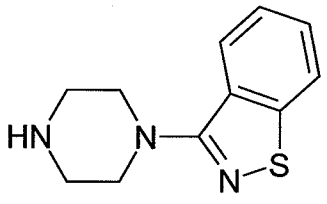
23. (Previously Presented): The compound of claim 22 wherein the R groups are independently methyl or ethyl.
24. (Previously Presented): The compounds of claim 23 wherein the R groups are all methyl or all ethyl.
25. (Previously Presented): A process for preparing ziprasidone of the formula I



---------- I

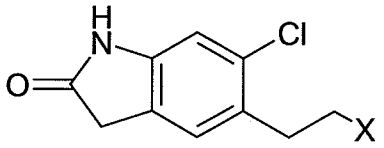
or a pharmaceutically acceptable salt thereof; or a solvate or a hydrate thereof;

which process comprises reacting 1-(1,2-benzisothiazol-3-yl)piperazine of the formula II:



---------- II

with 5-(2-haloethyl)-6-chloro-oxindole of the formula IV:

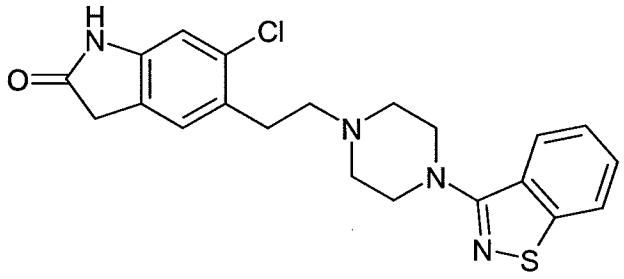


---------- IV

wherein X is fluoro, chloro, bromo or iodo;

in the presence of liquor ammonia and an alkaline metal carbonate or alkaline metal bicarbonate to form ziprasidone of the formula I; and optionally converting the ziprasidone formed into a pharmaceutically acceptable acid addition salt of ziprasidone, or a solvate or a hydrate thereof.

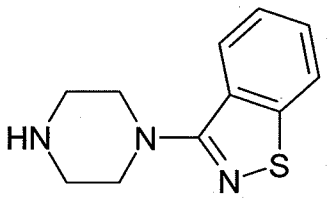
26. (Previously Presented): The process according to claim 25 wherein X of the formula IV is chloro, bromo or iodo.
27. (Previously Presented): The process according to claim 26 wherein X is Cl.
28. (Previously Presented): A process according to claim 1 further comprising controlling the mean particle size of ziprasidone, pharmaceutically acceptable acid addition salts of ziprasidone, and solvates and hydrates thereof formed in step (b) by a method of compacting using a compacting machine.
29. (Previously Presented): The process according to claim 28 wherein the pharmaceutically acceptable acid addition salt is ziprasidone hydrochloride.
30. (Previously Presented): The process according to claim 29 wherein the mean particle size of the product is about 80 microns or above.
31. (Previously Presented): A process for preparing ziprasidone of the formula I



---------- I

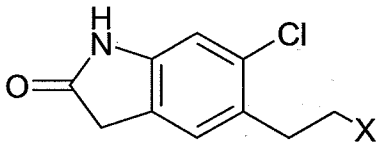
or a pharmaceutically acceptable salt thereof, or a solvate or a hydrate thereof,

which process comprises reacting 1-(1,2-benzisothiazol-3-yl)piperazine of the formula II:



---------- II

with 5-(2-haloethyl)-6-chloro-oxindole of formula IV:



---------- IV

wherein X is fluoro, chloro, bromo or iodo;

in the presence of pyridine and aqueous monomethylamine to form ziprasidone of the formula I and optionally converting the ziprasidone formed into a pharmaceutically acceptable acid addition salt of ziprasidone, or a solvate or a hydrate thereof.

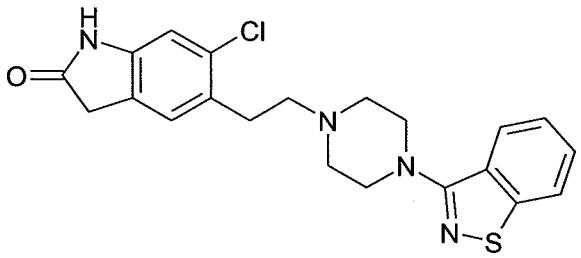
32. (Previously Presented): The process according to claim 31 wherein X of the formula IV is chloro, bromo or iodo.
33. (Previously Presented): The process according to claim 32 wherein X is chloro or bromo.
34. (Previously Presented): The process according to claim 33 wherein X is chloro.

35. (Previously Presented): The process according to claim 31 wherein the pharmaceutically acceptable salt is ziprasidone hydrochloride.

36. (Previously Presented): The process according to claim 31 wherein the hydrate is ziprasidone hydrochloride hemihydrate.

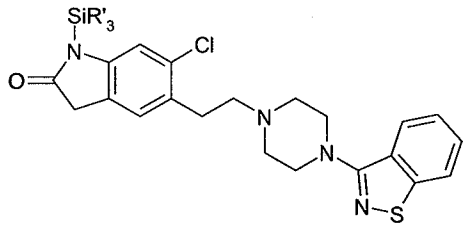
37. (Previously Presented): A process for purifyingf ziprasidone free base or a pharmaceutically acceptable acid addition salt of ziprasidone, or a solvate or a hydrate, the process comprising:

i) silylating crude ziprasidone of the formula I:



---------- I

with a silylating agent to form a silyl compound of the formula V:



-------- V

wherein R' groups are independently alkyl, and

ii) deblocking the silyl protecting group of the compound of the formula V formed in step (i) to precipitate ziprasidone of the formula I as ziprasidone free base or a pharmaceutically acceptable acid addition salt, or a solvate or a hydrate thereof as a crystalline salt.

38. (Previously Presented): The process according to claim 37 wherein the silylating agent is selected from trialkylsilyl halides, N,O-bis(trimethylsilyl)-acetamide and N,N'-bis(trimethylsilyl)-urea.

39. (Previously Presented): The process according to claim 38 wherein the trialkylsilyl halide is trialkylsilyl chloride.

40. (Previously Presented): The process according to claim 38 wherein the silylating agent is selected from trimethylsilyl chloride, triethylsilyl chloride, N,O-bis(trimethylsilyl)-acetamide and N,N-bis(trimethylsilyl)-urea.

41. (Previously Presented): The process according to claim 40 wherein the silylating agent is trimethyl silyl chloride.

42. (Previously Presented): The process according to claim 37 wherein the solvent used in the silylation step is selected from ethyl acetate, methyl acetate, isopropyl acetate, tert-butyl methyl acetate, ethyl formate, acetonitrile, dimethylsulfoxide, dioxane, benzene, toluene, xylene, methylene chloride, chloroform, carbontetrachloride, ethylene dichloride, acetone, methyl ethyl ketone, methyl isobutyl ketone, diethyl ketone, tert-butyl methyl ether, diethyl ether, diethyl carbonate and a mixture thereof.

43. (Previously Presented): The process according to claim 42 wherein the solvent used is selected from methylene chloride, ethylacetate, cyclohexane, ethylene dichloride, toluene, carbon tetrachloride and a mixture thereof.

44. (Previously Presented): The process according to claim 43 wherein the solvent is selected from methylene chloride, ethyl acetate, cyclohexane, ethylene dichloride and a mixture thereof.

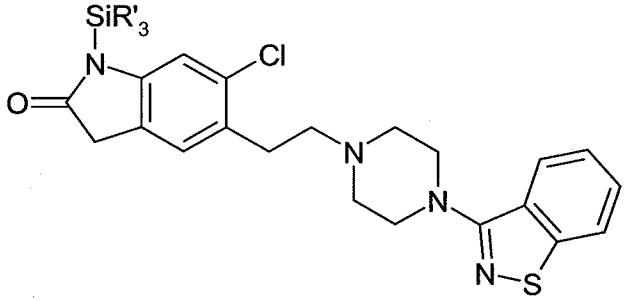
45. (Previously Presented): The process according to claim 37 wherein the silylation is carried out in the presence of a tertiary amine base.

46. (Previously Presented): The process according to claim 45 wherein the base is triethylamine, N,N-dimethyl-4-aminopyridine or trimethylamine.

47. (Previously Presented) The process according to claim 37 wherein the deblocking step(ii) is carried out by contacting the silyl compound of the formula V with a protic solvent, water or an acid for sufficient time to effect deblocking.

48. (Previously Presented): The process according to claim 47 wherein the protic solvent is an alcohol, and the acid is selected from hydrochloric acid, hydrobromic acid, hydroiodic acid and methanesulfonic acid.

49. (Previously Presented): The process according to claim 48 wherein the alcohol is ethanol or methanol.
50. (Previously Presented): The process according to claim 48 wherein the acid is hydrochloric acid.
51. (Previously Presented): The process according to claim 50 wherein ziprasidone is isolated as ziprasidone hydrochloride or hydrates thereof.
52. (Previously Presented): The process according to claim 51 wherein the hydrates of ziprasidone hydrochloride are ziprasidone hydrochloride hemihydrate or ziprasidone hydrochloride monohydrate.
53. (Previously Presented): The process according to claim 52 wherein the hydrate of ziprasidone hydrochloride is ziprasidone hydrochloride hemihydrate.
54. (Previously Presented): The process according to claim 48 wherein the protic solvent is methanol.
55. (Previously Presented): The process according to claim 47 wherein the solvent is water.
56. (Previously Presented): Compounds of the formula V:



---------- V

wherein the R^1 groups are independently alkyl.

57. (Previously Presented): The compounds as defined in claim 56 wherein the R^1_3 group is independently methyl or ethyl.
58. (Previously Presented): The compounds as defined in claim 57 wherein the R^1_3 group is methyl or all ethyl.
59. (Previously Presented): The process according to claim 11 wherein the solvent used in step(b) is selected from ethyl acetate, methyl acetate, isopropyl acetate, tert-butyl methyl acetate, ethyl formate, methanol, ethanol and isopropyl alcohol, acetonitrile,

tetrahydrofuran, dimethylformamide, dimethyl sulfoxide, dioxane, cyclohexane, n-hexane, benzene, toluene, xylene, methylene chloride, chloroform, carbontetrachloride, ethylene dichloride, acetone, methyl ethyl ketone, methyl isovutyl ketone, diethyl ketone, tert-butyl methyl ether, diethyl ether, diethyl carbonate, water and a mixture thereof.

60. (Previously Presented): The process according to claim 12 wherein the solvent used in step(b) is selected from ethyl acetate, methyl acetate, isopropyl acetate, tert-butyl methyl acetate, ethyl formate, methanol, ethanol and isopropyl alcohol, acetonitrile, tetrahydrofuran, dimethylformamide, dimethyl sulfoxide, dioxane, cyclohexane, n-hexane, benzene, toluene, xylene, methylene chloride, chloroform, carbontetrachloride, ethylene dichloride, acetone, methyl ethyl ketone, methyl isovutyl ketone, diethyl ketone, tert-butyl methyl ether, diethyl ether, diethyl carbonate, water and a mixture thereof.

61. (Previously Presented): The process according to claim 59 wherein the solvent is selected from dimethylformamide, methylisobutylketone, water or a mixture thereof.

62. (Previously Presented): The process according to claim 60 wherein the solvent is selected from dimethylformamide, methylisobutylketone, water or a mixture thereof.

63 Previously Presented): The process according to claim 28 wherein the pharmaceutically acceptable acid addition salt is ziprasidone hydrochloride and the hydrate is ziprasidone hydrochloride hemihydrate.

64. (Previously Presented): The process according to claim 63 wherein the mean particle size of the product is about 80 microns or above.

65. (Previously Presented): The process according to claim 28 wherein the pharmaceutically acceptable acid addition salt is ziprasidone hydrochloride and the hydrate is ziprasidone hydrochloride monohydrate.

66. (Previously Presented): The process according to claim 65 wherein the mean particle size of the product is about 80 microns or above.

67. (Previously Presented): A pharmaceutical composition comprising ziprasidone hydrochloride hemihydrate and ziprasidone hydrochloride monohydrate.